Genomic sequencing of human chromosome 19 and DNA repair genes.

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Utilizing a high-resolution, bacterial clone-based map of human chromosome 19, we have generated over 1.8 Mb of genomic sequence, targeted to selected regions of biological interest, including DNA repair gene regions in human and mouse. We have recently completed 184 kbp containing the human and rodent *XRCC1* and *ERCC2* genes, and have nearly completed 104 kbp containing the *HHR23A* gene in 19-p13.1. In addition to defining the structure of these DNA repair genes, we have identified 9 other genes in these regions, only one of which was known to map to 19. We have also completed the full-length cDNAs and corresponding genomic regions containing human *ERCC4* (chr 16) and*XRCC3* (chr 14); a P1 containing *XRCC2* (chr 7) is in progress.

Another sequencing target is an ~1 Mb region of 19q13.1 flanked by the genetic markers D19S208 and CANPS, which contains the candidate gene for an inherited congenital nephrotic syndrome (NPHSI). Sequence analysis of 15 cosmids identified 17 new genes, 7 of which appear to be novel, as well as 3 genes (APLP1, ATP4A, CD22) which had been previously mapped to this interval. The Alu retrotransposable element is highly represented (>1 Alu/kbp on average) in this region.

In 19p13.1, we sequenced 96.6 kbp to identify the nature of the polymorphism in cosmids which hybridized to the compound RFLP marker D19S11. In addition to the highly repetitive nature of the region, we identified 3 CYP4F subfamily genes, one of which appears to be the origin of the mRNA previously identified in polymorphonuclear leukocytes. Other regions of current sequencing activity include an ~100 kb region encompassing the MEF2B transcription enhancer factor in p13.1, a 250 kb contig containing multiple zinc finger genes from q13.4, and one cosmid containing 3 olfactory receptor genes from p13.1.

This work was performed by Lawrence Livermore National Laboratory under the auspices of the U.S. Department of Energy, Contract No. W-7405-Eng-48.